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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,663	10/16/2001	Jurgen Kleinschmidt	4121-123	9508

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,663	KLEINSCHMIDT ET AL.	
	Examiner	Art Unit	
	James L Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

Applicant's election with traverse of Group I, claims 1-8, in the paper filed 15 October 2003 is acknowledged. The traversal is on the ground(s) that one having the products of Groups I and III would have the products for the method of Group IV and that it is in the applicant's and the public's interest to disclose different "aspects" of the invention(s) in a single application. This is not found persuasive for the reasons of record and because the antibody product(s) of Group I do not necessarily share the features of the AAV vector of binding to a desired target cell other than an original target cell and the technical features of the antibody as claimed are not special for the reasons set forth in this Office action. However, search of the hybridoma of Group II with the antibodies of Group I was not found burdensome by the examiner and has been rejoined with the antibodies of Group I for consideration on the merits in this Office action. The requirement for restriction of the second product and its use from the antibodies and hybridomas of Groups I and II is still deemed proper and is therefore made FINAL.

Claims 10-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

This Application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this

application clearly fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825, particularly 37 CFR § 1.821(d). Applicants must direct the entry of "SEQ ID NO:" identifiers for every appearance of sequences in the description or claims of the patent application. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR § 1.821(g).

This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to for the reason that separate panels in Figs. 1 and 3 should be separately labelled. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Submission of corrected drawings may no longer be held in abeyance pending the indication of allowable subject matter. Failure to take corrective action within the set period will result in **ABANDONMENT** of the application. Direct any inquiries concerning drawing review to the Drawing Review Branch at (703) 305-8404.

The disclosure is objected to because of the following informalities: the brief description of drawings 1 and 3, and all reference to said drawings in the specification must indicate the panel of the Figure which is described or to which the reader is being referred, e.g. the Figures should be described and cited as Figure 1A or 1B, or Figure 3A or 3B or 3C. Appropriate correction is required.

Claims 4-9 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). However, in the interest of compact prosecution, the claims have been treated as if dependent upon claim 1 as appropriate.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-5 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification does not reasonably provide description of or enablement for any and every antibody population specific for adeno-associated virus which inhibits receptor binding other than antibody C24-B or C37-B, produced by

hybridomas DSMZ ACC 2369 or DSMZ ACC 2370. Applicant provides guidance only for the above noted monoclonal antibodies and provides no guidance as to what modifications or structure are important for the predictable function of any other monospecific antibody. Very different structures may be found on antibodies with the same specificity. For example, very different variable heavy (V_H) chains can combine with the same variable light (V_L) chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different specificities. In the absence of any guidance other than to the use of the C24-B or C37-B antibodies, one would not know or be able to predict or envision what structure or modifications were important for function. Moreover, applicant provides guidance only for immunization with particular peptides and capsids from AAV-2, it is not known if the two exemplified antibody species bind to any of these peptides as part of their epitope(s), and one would not readily know, absent any description or guidance from applicant, peptides which predictably elicit neutralizing antibodies for any of the other listed AAVs. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that a molecule is part of the invention and a reference to a potential method of isolating

it. The molecule itself is required. Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of molecules by only their functional activity does not provide an adequate written description of the genus. The court indicated that although applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Applicant is reminded that the written description provision of 35 USC 112 is severable from its enablement provision. However, in view of the guidance in the instant specification to two particular species of unknown relationship, the amount of experimentation required to determine functional structures or modifications for other usable species would also be undue. For example, as noted above, very different structures may be found on antibodies with the same specificity, and conversely, similar structure may be found on antibodies having different specificities and one would not know, given the instant guidance and absent further unguided experimentation, what variable region changes would predictably function in the invention other than those possessing both the intact V_H and V_L chains of the C24-B or C37-B antibody or what immunogens to use for any AAV other than AAV-2. Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

The specification is objected to and claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

It is unclear if cell lines which produce antibodies having the exact chemical identity and properties of the antibodies designated C24-B or C37-B, produced by hybridomas DSMZ ACC 2369 or DSMZ ACC 2370, are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: the claimed cell line; the cell lines which produce the chemically and functionally distinct antibodies claimed; and/or, the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event. As noted above, very different structures may be found on antibodies with the same specificity, and conversely, similar structure may be found on antibodies having different specificities. Therefore, it would require undue experimentation to reproduce the claimed monoclonal antibody species chemically as produced by the hybridomas designated DSMZ ACC 2369 or DSMZ ACC 2370. A

suitable deposit of the hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the biological materials will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) the deposits were viable at the time of deposit; and,
(e) the deposits will be replaced if they should ever become non-viable.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-9, "characterized in that" is improper claim language and is vague as to what is encompassed because it is not clear if "characterized" is open or closed claim language and therefore the term does not clearly set forth the metes and bounds of the invention for which applicant desires protection. In these claims "the" capsid, binding, or receptor lack antecedent basis.

In claims 5-9, "the region" and "the...proteins" lack antecedent basis. These claims are vague and indefinite because it is not clear if the parenthetical recitation of "based on VP-1" is intended as a limitation or is merely exemplary of "region." It is not clear how the region is "based on" VP-1.

Claims 6-9 are vague and indefinite because it is not clear if the parenthetical recitations of deposit numbers are intended as a limitation. The claims should positively recite the deposit accession numbers to clearly identify the antibodies/hybridomas because, absent their recitation, it is not clear what structure and properties are encompassed by the named antibodies.

In claims 7-9, it is not clear what is encompassed by a "desired" ligand because the function or properties necessary for a ligand to be desirable are not clear.

In claims 8 and 9, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

Regarding claims 8 and 9, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claims 1-4 and 7-9 are rejected under 35 U.S.C. § 102(a) as being anticipated by Bartlett et al. (Nature Biotechnol. 17: 181, 1999) in light of the disclosure of Patel et al. (U.S. Pat. No. 6,498,244).

Bartlett et al. disclose the A20 anti-adeno-associated virus capsid monoclonal antibody, which in light of Patel et al. is a neutralizing antibody which binds to sequences common to VP1, VP2, and VP3 (see e.g. cols. 4 and 5). The reference also discloses a conjugate of A20 with another antibody specific for a different cell surface receptor to direct a virus vector to a normally nonpermissive cell and to inhibit infection in normally permissive cells.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 29 October 1998. It is noted, however, that applicant has not filed a certified copy of the German 198 49 643.5 application as required by 35 U.S.C. 119(b). Moreover, applicant

cannot rely upon the filing of the foreign priority papers to overcome this rejection because a translation of said papers has also not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 1-4 and 7-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wistuba et al. (J. Virol. 69: 5311, 1995) in light of the disclosure of Patel et al. (U.S. Pat. No. 6,498,244).

Wistuba et al. (see e.g. pages 5315-5316) disclose the A20 anti-adeno-associated virus capsid monoclonal antibody, which in light of Patel et al. is a neutralizing antibody which binds to sequences common to VP1, VP2, and VP3 (see e.g. cols. 4 and 5).

Claims 1-4 and 7-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kern et al. (WO 95/11997) in light of the disclosure of Patel et al. (U.S. Pat. No. 6,498,244).

Kern et al. (see e.g. page 3) disclose the A20 anti-adeno-associated virus capsid monoclonal antibody, which in light of Patel et al. is a neutralizing antibody which binds to sequences common to VP1, VP2, and VP3 (see e.g. cols. 4 and 5).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having

ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-9 are rejected under 35 U.S.C. 102(e)(2) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Patel et al. (U.S. Pat. No. 6,498,244).

Patel et al. disclose the A20 anti-adeno-associated virus capsid monoclonal antibody which binds to sequences common to VP1, VP2, and VP3 (see e.g. cols. 4 and 5). The reference also discloses peptide epitopes bound by other neutralizing antibodies, including other neutralizing monoclonal antibodies. The neutralizing monoclonal antibodies of the reference appear to anticipate the antibodies as instantly claimed. However, if not, the reference provides guidance to a number of epitopes bound by neutralizing antibodies which would reasonably guide one of ordinary skill in the art to the elicitation of other antibodies with similar properties. Further, the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon

applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
June 23, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641